UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,193	01/31/2002	Brian Hicke	NEX86/PCT-US	6209

25871 7590 01/30/2004

SWANSON & BRATSCHUN L.L.C.
1745 SHEA CENTER DRIVE
SUITE 330
HIGHLANDS RANCH, CO 80129

EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,193	HICKE ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33 and 44-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33 and 44-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1/02 12/02 11/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 12 November 2003 in which claim 33 was amended, claims 1-32 and 34-43 were canceled and claims 44-58 were added. All of the amendments have been thoroughly reviewed and entered. The previous objections and rejections in the Office Action dated 12 August 2003 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

The examiner for this application has changed. Please address future correspondence to Examiner BJ Forman, Art Unit 1634.

Claims 33 and 44-58 are under prosecution.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see e.g. page 21, line 11). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

First paragraph of 35 U.S.C. 112: Enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 33 and 44-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

While the specification is enabling for a method of selecting tenascin-C nucleic acid ligands from U251 human glioblastoma cells (Examples 1-2) and for methods for detecting tenascin-C in xenograft tissues in mice using a tenascin-C-specific nucleic acid ligand i.e. TTA 1 (Example 4) wherein the TTA1 ligand detected tenascin-C in three different tumor cell lines glioblastoma, breast, colorectal, and rhabdomyosarcoma (Fig. 6), the specification does not enable one skilled in the art to which it pertains or with which it is most nearly connected to make or use the invention commensurate in scope with the claims. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirements and whether undue experimentation would be required to make and use the claimed invention (see *In re Wands*, 858 F. 2d 731, 737, 8 USPQ 2d 1400, 1404, 1988). These factors include but are not limited to:

Breadth of the Claims

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

The claims are written so broadly so as to encompass any cancerous disease in any tissue or organism using any nucleic acid ligand. The claimed cancers include a wide variety of cancers including any of the large genus of epithelial cancers, hemopoietic, immune system, central nervous system and connective tissue cancers. The broadly drawn method also encompasses detection of cancers in the vary large genus of organisms using a very large genus of nucleic acid ligands.

The specification teaches a method of selecting tenascin-C nucleic acid ligands from U251 human glioblastoma cells (Examples 1-2) and for methods for detecting tenascin-C in xenograft tissues in mice using a tenascin-C-specific nucleic acid ligand i.e. TTA 1 (Example 4) wherein the TTA1 ligand detected tenascin-C in three different tumor cell lines glioblastoma, breast, colorectal, and rhabdomyosarcoma (Fig. 6). However, the specification also teaches that tenascin-C is expressed in a variety of non-diseased tissues e.g. liver, lung, spleen, intestine, kidney (Fig. 7). Because the claims are so broadly drawn to detecting disease by detecting a tenascin-C nucleic acid ligand, because the specification merely teaches detection of a few types of cancer using a single tenascin-C nucleic acid ligand; and because the specification teaches tenascin-C expression in non-disease tissue, the specification is not enabling for the broadly claimed invention.

Nature of the Invention

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

The nature of the invention is such that detecting a disease using a ligand would require a teaching of a relationship between the ligand and the disease wherein the teaching would minimally include an illustration or examples of the relationship the ligand and the disease e.g. sample population studies illustrating that tenascin-C expression detects cancer regardless of the amount, time or pattern of expression.

The specification does not provide a teaching such a relationship. The specification teaches that tenascin-C is expressed in three different tumor cell lines glioblastoma, breast, colorectal, and rhabdomyosarcoma (Fig. 6) but the specification also teaches that tenascin-C is expressed in non-diseased tissues e.g. liver, lung, spleen, intestine, kidney (Fig. 7). The specification does not teach an amount of tenascin-C expression indicative of disease or a temporal pattern of tenascin-C indicative of disease.

While the specification teaches a relationship between tenascin-C and the nucleic acid specific for it, the specification does not teach a relationship between tenascin-C and diseases of cancer, psoriasis and atherosclerosis which would enable one of skill in the art to make and use the invention as claimed.

Level of Predictability in the Art

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

The level of predictability in the art is very low with regard to detection of disease without a correlating relationship between the disease and the detecting molecule. Because the relationship between tenascin-C expression and cancer, psoriasis or atherosclerosis is unknown and because tenascin-C is expressed in non-diseased tissue (Fig. 7), the level of predictability that detection of tenascin-C would detect disease is very low. Therefore, the level of predictability in the art is very low with regard to detecting tenascin-C to detect a disease.

Existence of Working Examples

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

The specification teaches a method of selecting tenascin-C nucleic acid ligands from U251 human glioblastoma cells (Examples 1-2); the specification provides working examples of detecting tenascin-C in xenograft tissues in mice using a single tenascin-C-specific nucleic acid ligand i.e. TTA 1 (Example 4); the specification teaches TTA1 detection of tenascin-C in three different tumor cell lines glioblastoma, breast, colorectal, and rhabdomyosarcoma (Example 5 and Fig. 6). However, the specification also teaches that tenascin-C is expressed in a variety of non-diseased tissues e.g. liver, lung, spleen, intestine, kidney (Example 7 and Fig. 7). The specification does not provide working examples of the broadly claimed invention i.e. detection of cancer, psoriasis and atherosclerosis by detecting a tenascin-C nucleic acid ligand. Therefore, the specification does not provide working examples of the claimed invention which would enable one of ordinary skill in the art to make and use the invention as claimed.

Quantity of Experimentation Required

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand.

In view of the breadth of the claims being drawn to detecting a large genus of diseases by detecting any of a large genus of tenascin-C nucleic acid ligands; in view of the nature of the invention in which detecting a disease would require a teaching of a relationship between the disease and the ligand being detected and the lack of a teaching in the specification of the relationship; in view of the of unpredictability in the art with regard to detecting a disease without a correlating relationship between the disease and the detecting molecule; and in view of the lack of working examples of the broadly claimed invention, it would require undue experimentation for one skilled in the art to make and use the invention as claimed.

Second paragraph of 35 U.S.C. 112: Indefinite

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 33 and 44-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33 and 44-58 are indefinite in Claim 33 because the claim is drawn to a method for detecting a disease but the method steps do not include a step for disease detection. Therefore, it is unclear whether the method steps achieve the claimed method.

Claim 50 is indefinite because it is unclear whether the sequences of Tables 3, 4 and Figure 2 are the same or different from SEQ ID NO: 4-65.

Claim 55 is indefinite because it appears to use symbols which are different from those of claim 54. Specifically, Claim 54 defines "5" as 3'-3'dT and illustrates the terminus of the complex as "5" while Claim 55 illustrates the same complex but identifies the terminus as 3'-3'-T. Additionally, Claim 54 identifies "6" as 2'Ome G and illustrates the second from terminus as "6" while Claim 55 illustrates the same complex but identifies the same position as "G" and limits all Gs to 2'-OMe modified. Because Claims 54 and 55 use different symbols to identify the same positions, the claims are confusing and therefore indefinite.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The claims are drawn to a method for detecting a disease selected from cancer, psoriasis and atherosclerosis wherein the method comprises detecting the presence of a tenascin-C nucleic acid ligand. The specification is not enabling for the scope of the claimed invention. However, the specification is enabling for a method of selecting tenascin-C nucleic acid ligands from U251 human glioblastoma cells (Examples 1-2) and for methods for detecting

tenascin-C in xenograft tissues in mice using a tenascin-C-specific nucleic acid ligand i.e. TTA 1 (Example 4). Hicke et al teaches this embodiment of the claimed invention as detailed below.

8. Claims 33, 44-55 and 57-58 are rejected under 35 U.S.C. 102(a) as being anticipated by Hicke et al (J. Nuc. Med. May 1999, 40(5):99) as defined by Hicke (slide presented by Brian Hicke 7-10 June 1999)

Regarding Claim 33, Hicke et al disclose a method for detecting the presence of cancer in a biological tissue comprising attaching a marker to a tenascin-C nucleic acid ligand to from a marker-ligand complex, exposing the complex to the biological tissue and detecting the presence of the complex (third paragraph).

Regarding Claims 44-46, Hicke et al disclose the method wherein the marker is TC-99m (third paragraph, line 4).

Regarding Claim 47, Hicke et al disclose the method wherein the ligand comprises a linker i.e. TTA 1 (as illustrated on the Slide presented by Brian Hicke).

Regarding Claim 48, Hicke et al disclose the method wherein the linker is $(CH_2CH_20)_6$ i.e. TTA 1 (as illustrated on the Slide presented by Brian Hicke).

Regarding Claim 49, Hicke et al disclose the method wherein the linker has the claimed structure i.e. TTA 1 (as illustrated on the Slide presented by Brian Hicke).

Regarding Claims 50-55, Hicke et al disclose the method wherein the ligand is from the claimed group i.e. TTA 1 (as illustrated on the Slide presented by Brian Hicke).

Regarding Claim 57, Hicke et al disclose the method wherein the disease is cancer (page 99, third paragraph).

Regarding Claim 58, Hicke et al disclose the method wherein the ligand is identified by the claimed method i.e. via SELEX (page 99, first paragraph).

Conclusion

9. No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741 until 13 January 2004. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-0507.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
January 27, 2004